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10/581,703	06/02/2006	Stefan Muhlbauer	049202/310397	3618

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EXAMINER
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KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
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1638

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/581,703	<b>Applicant(s)</b> MUHLBAUER, STEFAN	
	<b>Examiner</b> Anne R. Kubelik	<b>Art Unit</b> 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 1/22/08.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 30-42 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 June 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. Applicant's election of Group II (claims 6-8, 10-21, 23, 30 and claims 1-5, 9, 22, 24-28 and 31-42 to the extent they read on a process of controlling plastid expression by external application of a chemical control signal) in the reply filed on 22 January 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 29, and the portions of claims 1-28 and 30-42 drawn to physical signals are withdrawn from consideration as being drawn to nonelected inventions.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from the sequences in ¶3 on pg 32, ¶1 on pg 33, ¶1 on pg 36, ¶2 on pg 39, ¶2 on pg 42, ¶ 2 on pg 2, and ¶2 on pg 44.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth herein. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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4. Claims 1-2, 6, 20, 22-28 and 30-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims require nucleic acids that encode translation regulatory RNAs. The only such RNAs described in the specification, via Suess et al (2004, Nuc. Acids Res. 32:1610-1614) are RNA apamers. The specification fails to describe the structural features of any translation regulatory RNAs that are not RNA apamers.

Hence, Applicant has not, in fact, described nucleic acids that encode translation regulatory RNAs within the full scope of the claims. Because the nucleic acids are not described, the method of using the sequences to controlling the expression of a plastome-encoded sequence of interest in a plant is likewise not described, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the compositions used in the claimed methods, Applicant does not appear to have been in possession of the claimed genus at the time this application was filed.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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6. Claims 6, 9 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 6 recites the broad recitation "chemical signal or a source thereof", and the claim also recites "non which is the narrower statement of the range/limitation. Claim 9 recites the broad recitation "transcription regulatory sequence", and the claim also recites "heterologous" which is the narrower statement of the range/limitation. Claim 16 recites the broad recitation "phytopathogen", and the claim also recites "*Agrobacterium*" which is the narrower statement of the range/limitation.

***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-2, 6, 9-13, 15-18, 26, 30, 32-34 and 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by McBride et al (1999, US Patent 5,925,806).

McBride et al claim a method comprising exposing, by direct application, a plant to a chemical activating compound, wherein the nuclei of said plant are transformed with a construct comprising, as operably linked components, a promoter inducible by the chemical, a nucleic acid encoding a plastid transit peptide, a nucleic acid encoding a T7 RNA polymerase, and a transcription terminator, the plastids of said plant transformed with a construct comprising, as operably linked components, a promoter specific for the T7 RNA polymerase, a nucleic acid encoding a protein of interest, and a transcription terminator, thereby inducing expression of the sequence of interest (claim 15; see also column 14, line 7, to column 16, line 13).

Upon expression of the T7 polymerase in the nucleus and its subsequent transport to the chloroplast, the T7 polymerase transcribes the sequence of interest from the T7 polymerase promoter (column 12, line 54, to column 13, line 6)3. The nuclear promoter includes tissue-specific and developmentally regulated promoters (claims 3-10). The nuclear construct is introduced by Agrobacterium-mediated transformation, and thus would be externally applied by Agrobacterium (column 10, lines 22-40). The claims are also drawn to the control signal being a source of the chemical signal (claim 16).

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9. Claims 1-6, 9-11, 19, 26, 28, 30-31, 33-39 and 41-42 are rejected under 35 U.S.C. 102(b) as being anticipated by McBride et al (WO 01/02593).

McBride et al teach a method comprising exposing, by direct application, a plant to a chemical activating compound, acetylated homoserine lactone (AHL), wherein the chloroplasts of said plants are transformed with a construct comprising the GUS coding sequence (the sequence of interest) expressed under control of the luxI promoter/operator and the luxR protein (pg 43, paragraph 3, to pg 45, paragraph 1; pg 50, paragraphs 1-4; claims 17-22; Fig. 19-23). The luxI promoter is an AHL-response element, and AHL is a nonproteinoaceous chemical signal. In this arrangement, AHL activated the luxR protein, changing its binding affinity to luxI, activating expression of GUS; the luxR protein is not involved in expression of other plastid sequences. The regulatory protein also encoded on the construct (Fig 19-22). LuxR is of prokaryotic origin.

### ***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 1-11, 17-19, 26-28, 30-31, and 33-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (WO 01/02593 in view of Maliga (1996, US Patent 5,530,191).

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The claims are drawn to a method of controlling the expression of a plastome-encoded sequence of interest in a plant by externally applying to a plant a chemical signal that controls expression of the sequence of interest via the tet or lac operators/repressors.

The teachings of McBride et al are discussed above. McBride et al do not teach use of the tet or lac operators.

Maliga teaches a method controlling expression of plastome-encoded sequence of interest, wherein plants, whose nuclei are transformed with construct comprising a nuclear promoter operably linked to a sequence encoding a plastid transit peptide operably linked to a regulator polypeptide, and whose plastids are transformed with a construct comprising a male-sterility gene (the sequence of interest) under control of the regulator polypeptide (claims 1, 3-7). The regulator polypeptide includes the T7 polymerase (claim 10). The plastid construct can comprise a target sequence for preventing gene expression, regulated by, for example, the lac or tet repressor (claims 16, 27-31)

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of controlling the expression of a plastome-encoded sequence of interest in a plant by externally applying to a plant a chemical signal that controls expression of the sequence of interest as taught by McBride et al, to substitute the tet or lac operators/repressors described in Maliga for the luxI promoter/operator. One of ordinary skill in the art would have been motivated to do so because substitution of one type of operator system for another is an obvious design choice. Further, McBride et al teaches that the tetR system is analogous to the luxR system (pg 18, paragraph 2). One of ordinary skill in the art would have



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substituted IPTG or tetracycline for AHL because these are the chemical controls for the lac and tet operator/repressors, respectively.

12. Claims 1-6, 9-11, 19-26, 28, 30-31, 33-39 and 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (WO 01/02593) in view of Suess et al (2004, Nuc. Acids Res. 32:1610-1614).

The claims are drawn to a method of controlling the expression of a plastome-encoded sequence of interest in a plant by externally applying to a plant a chemical signal that controls expression of the sequence of interest, wherein the sequence of interest is operably linked to a translation regulatory RNA aptamer adapted for binding the chemical signal.

The teachings of McBride et al are discussed above. McBride et al do not teach use of translation regulatory RNA apamers as the expression control system.

Suess et al teach a translation regulatory RNA apamer adapted for binding a chemical signal (theophylline) and thus controlling translation of a sequence of interest (lacZ) (pg 1611, right column, paragraph 5, to pg 1612, right column, paragraph 2).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of controlling the expression of a plastome-encoded sequence of interest in a plant as taught by McBride et al to substitute the RNA apamer described in Suess et al for the luxI promoter/operator. One of ordinary skill in the art would have been motivated to do so because choice of one control system that works in a bacterial or bacterial-like system, as are chloroplasts, over another is a design choice dependent upon the preference of the practitioner.

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13. Claims 1-2, 6, 9-18, 26, 30, 32-34 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (1999, US Patent 5,925,806).

The claims are drawn to a method of controlling the expression of a plastome-encoded sequence of interest in a plant by externally applying to a plant a chemical signal that controls expression of the sequence of interest, wherein the control signal is encoded by a nucleic acid that was introduced into the plant via a viral vector.

The teachings of McBride et al are discussed above. McBride et al do not teach introduction of the nucleic acid by RNA viral vector.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of controlling the expression of a plastome-encoded sequence of interest as taught by McBride et al to introduce the nuclear construct into the plant via a viral vector rather than by Agrobacterium-mediated transformation. One of ordinary skill in the art would have been motivated to do so because selection of one method of transformation over another is a design choice that does not provide patentable distinction to the method.

### ***Conclusion***

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is

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Anne Kubelik, Ph.D.

April 11, 2008

/Anne R. Kubelik/

Primary Examiner, Art Unit 1638